I. CASE HISTORY

JK is a 27 year old female who is pregnant with her second child and presents to her obstetrician for the first prenatal visit of this pregnancy. She delivered her first child 4 years ago at 39 weeks with no complications.

Routine prenatal testing is ordered including ABO, Rh(D), and antibody screen.

Sample EDU -03 Patient Red Blood Cells

Sample EDU -04 Patient Serum

II. EXPECTED RESULTS

	ABO / Rh(D)	Antigen Type
Sample EDU- 03	A POS	E negative, c (small) negative

	ABO	Antibody Screen	Antibody ID
Sample EDU- 04	A	POS	Anti-E, Anti-c (small)

III. DISCUSSION

A Discussion of the Rh System

History

The Rh system was first described in 1939 when a woman experienced a severe transfusion reaction following transfusion of ABO compatible blood from her husband. She had delivered a stillborn child with erythroblastosis fatalis and her serum agglutinated red blood cells from her husband and most ABO compatible donors.[1] A year later, Landsteiner and Wiener reported similar rates of incompatibility (85%) in sera from rabbits that were stimulated with red blood cells from *Macacus rhesus* monkeys. As a result, Landsteiner and Wiener hypothesized that a common factor (Rh) was present on both human and rhesus red blood cells to which the antibodies (anti-Rh) produced by the animals and in the human case reported a year earlier were directed against.[2] Although the Rh and anti-Rh nomenclature were proven incorrect in 1943[3] and the antibody name was changed to anti-D,[4] Rh and anti-Rh continued to be commonly used. In 1941, two more antigens were added to the Rh system: C, described by Weiner[5], and c, described by Levine.[6] In 1943, the E antigen was described[7,8] and added to the Rh system and the e antigen was added in 1945.[9]

Today the Rh system is a complex group of 54 different specificities of red blood cell antigens.[10]

Rh System Antigens

D	C	E	c	e	f	Ce	C^w
C^x	V	E^w	G	Hr_o	Hr	hr^S	VS
C^G	CE	D^w	c-like	cE	hr^H	Rh29	Go^a
hr^B	Rh32	Rh33	Hr^B	Rh35	Be^a	Evans	Rh39
Tar	Rh41	Rh42	Crawford	Nou	Riv	Sec	Dav
JAL	STEM	FPTT	MAR	BARC	JAHK	DAK	LOCR
CENR	CEST	CELO	CEAG	PARG	CEVF		

Genetics

The antigens of the Rh system are encoded by two genes, RHD and RHCE, inherited as codominant alleles.[11] The RHD gene produces the RhD protein which carries the D antigen and the RHCE gene produces the RhCE protein which carries the C,c,E,e antigens as well as many other Rh antigens.

Frequencies of the five primary Rh antigens[12]

	Caucasian	African-American	Asian
D	85%	92%	99%
C	68%	27%	93%
E	29%	22%	39%
c	80%	96%	47%
e	98%	98%	96%

Clinical Significance

Following the ABO system, the Rh system is the most recognized and clinically significant blood group system. The five primary Rh antigens (D, C, c, E, and e) represent most of the clinically significant antibodies in the system and the D antigen is the most immunogenic antigen outside of the ABO system.

D > c > E > C > e

A comparison of the immunogenicity of the five primary Rh antigens[13]

Hemolytic Disease of the Fetus and Newborn (HDFN)

Most often resulting from a fetomaternal hemorrhage (FMH) during placental separation at the time of delivery,[14] immunization associated with pregnancy occurs when fetal red cells expressing a paternal antigen enter the maternal circulation. It is estimated that FMH of varying degrees occurs in up to 75% of pregnancies.[15]

In later pregnancies, these maternal antibodies may cross the placenta into fetal circulation and attach to corresponding paternal antigens on fetal red cells. These cells are then removed from fetal circulation by macrophages in the reticuloendothelial system, particularly in the spleen. The rate of red cell destruction is influenced by the antibody titer and the number of antigen sites on the fetal red cells. If the fetal bone marrow fails to produce sufficient red cells to compensate for the rate of red cell destruction, fetal erythropoiesis outside the bone marrow is increased in the hematopoietic tissues of the liver and spleen. These organs become enlarged resulting in portal hypertension and hepatocellular damage.

The diagnosis and management of HDFN requires collaboration between the patient, obstetrician and the blood bank. Rh system antibodies are the most common alloantibodies detected in routine antibody screen testing during pregnancy.[16-20] When a clinically significant antibody is identified in maternal serum, the fetus is typically monitored with a combination of antibody titers and ultrasounds. Further decisions on how and when to treat an affected fetus are based on the degree of fetal anemia and gestational age.

References

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